Notice of Allowability	Application No.	Applicant(s)	
	09/854,412	CONRAD, RICHARD C.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the Request for Continued Examination filed February 4, 2004*.

2. ☒ The allowed claim(s) is/are *1-36 and 61*.

3. ☒ The drawings filed on *11 May 2001* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Gina Shishima on April 15, 2004.

The application has been amended as follows:

In the specification-

Please substitute the following for the paragraphs beginning on page 8, line 25 and ending on page 9, line 28 of the specification:

In some embodiments of the invention, a composition comprising a sample, poly(dT) nucleic acid molecule, and an isostabilizing agent may first be heated at a temperature between about 60°C and about 90°C, or between about at least 70°C and about 90°C, prior to incubation under hybridization conditions. Temperatures of about 60°C, 70°C, 80°C, and 90°C are specifically contemplated. In some embodiments, hybridization conditions comprise incubating the composition between about 15°C and 50°C for at least 3 minutes to 48 hours, or at least 10 minutes to 48 hours, though longer times are contemplated insofar as substantial RNA degradation does not occur. In additional embodiments, incubation time for hybridization is at least 20 minutes, 1 hour , 4 hours, or 8 hours. During hybridization or binding, the sample may be gently rocked.

Furthermore, in some embodiments, the binding solution or a solution containing an isostabilizing agent is discarded and additional solution added to the sample; this may be done multiple times.

Methods of the present invention also include a wash step in some embodiments. Poly(A) RNA may be washed one, two, three, four, five, six, seven, eight, nine, ten, or more times. The wash step may be implemented before or after excess liquid from the sample and/or binding solution is removed. The wash step involves incubating the poly(dT) nucleic acid and poly(A) RNA hybridized to it with a wash solution. In some embodiments, the wash solution contains an isostabilizing agent, such as TMAC or TEAC in a concentration less than its concentration in the composition exposed to hybridization conditions or in the binding solution. The final concentration of the isostabilizing agent during a wash step of a composition comprising poly(A) RNA will be about 0.05 M to about 3.0 M; in some embodiments, the final concentration is below about 0.5 M (low salt wash solution), while in others it is greater than about 2.0 M (high salt wash solution) (medium salt wash solution is between 0.5 M and 2.0 M). A final concentration of the isostabilizing agent during the wash step is specifically contemplated to be 0.4 M. In a specific embodiment the poly(dT) or poly(U) nucleic acid molecule and the hybridized poly(A) RNA are washed at least once in a wash solution with an isostabilizing agent concentration greater than about 1.2 M and at least once in a wash solution with an isostabilizing agent concentration of less than about 0.5 M. In further embodiments, a sample is washed with a low, medium, and/or high salt wash solution. As discuss above, the wash solution may be diluted from a higher concentration, for

example, 2x (or 2X) concentration, to a final concentration of 1x. Thus, for example, in one embodiment of the invention, a 2X binding solution containing 4 M TMAC and .035% Triton X-100 is mixed with an equal volume of sample to achieve a final concentration for hybridization reaction of 2 M TMAC and 0.017% Triton X-100. In many embodiments of the invention, the final concentration of an isostabilizing agent during the binding step is higher than the final concentration of an isostabilizing agent during the wash step.

In the claims-

Please cancel claims 37-60.

Please amend claim 31 as follows:

31. A method for purifying poly(A) mRNA from a sample in a manner that reduces rRNA carryover comprising:

a) incubating the sample with a poly(dT) oligonucleotide connected to a non-reacting structure and a hybridization solution comprising ~~tetramethylammonium~~ TMAC and/or TEAC under conditions allowing poly(A) mRNA to hybridize with the oligonucleotide;

b) isolating the oligonucleotide with the hybridized poly(A) mRNA away from the sample; and

c) washing the oligonucleotide with a wash solution comprising a salt wherein rRNA carryover is reduced.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JAMES KETTER
PRIMARY EXAMINER